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Policy Number: 056.000

Title: Coverage Determination Policy for Cabotegravir/Rilpivirine (Cabenuva)

Regions: ☒ **Texas** ☐ **Florida** ☐ **Indiana** ☐ **New Jersey** ☒ **New Mexico**

Impacted Areas:

- ☒ Network Management/Provider Services
- ☐ Member services
- ☐ Quality Management
- ☐ Credentialing
- ☐ IT
- ☐ Administration
- ☐ Compliance/delegation
- ☒ Utilization Management
- ☐ Case management
- ☐ Disease management
- ☒ Claims
- ☐ Human resources
- ☐ Finance
- ☒ Pharmacy
- ☐ ALL

Available LCD/NCD/LCA: NONE

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Doctors helping patients for more than 25 years

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Coverage Policy Number: 056.000

Line of Business: Medicare Part B

Policy Type: Prior Authorization

Coverage Determination:

Initial/New Requests

This policy refers to the following long-acting injectable antiretroviral products: **Cabenuva (cabotegravir/rilpivirine)**

Cabenuva (cabotegravir/rilpivirine) Cabenuva (cabotegravir/rilpivirine) is proven for the treatment of a **human immunodeficiency virus type-1 (HIV-1)** in patients who are virologically suppressed (HIV-1 RNA less than 50 copies per mL). Cabenuva is medically necessary when the following additional criteria are met:

For initial therapy, **ALL** of the following:

A. Diagnosis of HIV-1 infection
B. Patient has no prior virologic failures or baseline resistance to either cabotegravir **OR** rilpivirine
C. Patient is currently on a stable antiretroviral regimen
D. Submission of medical records (e.g., chart notes, laboratory results) showing viral suppression (HIV-1 RNA less than 50 copies per mL) for at least 3 months prior to initiation of Cabenuva
E. Provider attests that patient demonstrates treatment readiness by **BOTH** of the following:
    i. Patient understands the risks of missed doses of Cabenuva
    ii. Patient has the ability to adhere to the required monthly or every 2 months injection appointments
F. Dosing is in accordance with the United States Food and Drug Administration approved labeling
G. Cabenuva will be approved for duration as determined through clinical review.

Note: *Cabenuva is unproven and* ***NOT*** *medically necessary for the treatment of human immunodeficiency virus type-1 (HIV-1) in patients who are not currently virally suppressed (HIV-1 RNA less than 50 copies per mL).*

Renewal/Continuation of Therapy Requests

For continuation therapy, **ALL** of the following:

A. Patient has previously received treatment with Cabenuva
B. Provider confirms that the patient has achieved and maintained viral suppression (HIV-1 RNA less than 50 copies per mL) while on Cabenuva therapy
C. Dosing is in accordance with the United States Food and Drug Administration approved labeling
D. Cabenuva will be approved for duration as determined through clinical review.

Note: *Cabenuva is unproven and* ***NOT*** *medically necessary for the treatment of human immunodeficiency virus type-1 (HIV-1) in patients who are not currently virally suppressed (HIV-1 RNA less than 50 copies per mL).*

FDA Approved Dose and Indication

Indication	Approved Dosing
HIV infection, to replace current stable antiretroviral regimen	**Monthly dosing:** cabotegravir 600mg/rilpivirine 900mg on last day of current antiretroviral therapy or oral lead-in then continue with cabotegravir 400mg/rilpivirine 600mg every month thereafter **Every 2 month dosing:** cabotegravir 600mg/rilpivirine 900mg on last day of current antiretroviral therapy or oral lead-in for 2 consecutive months then continue with cabotegravir 600mg/rilpirvirine 900mg every 2 months

General Background

Cabenuva (cabotegravir/rilpivirine) is a 2-drug co-packaged product of extended-release injectable suspension formulations of cabotegravir, a human immunodeficiency virus type-1 (HIV-1) integrase strand transfer inhibitor (INSTI), and rilpivirine, an HIV-1 non-nucleoside reverse transcriptase inhibitor (NNRTI). Cabotegravir inhibits HIV integrase by binding to the integrase active site and blocking the strand transfer step of retroviral deoxyribonucleic acid (DNA) integration which is essential for the HIV replication cycle. Rilpivirine is a diarylpyrimidine NNRTI of HIV-1 and inhibits HIV-1 replication by non-competitive inhibition of HIV-1 reverse transcriptase (RT).[1]

Clinical Evidence

The efficacy of Cabenuva has been evaluated in three Phase 3 randomized, multicenter, active-controlled, parallel-arm, open-label, non-inferiority trials:[1-3]

1. Trial 201584 (FLAIR, [NCT02938520]), (n = 629): HIV-1–infected, antiretroviral treatment (ART)-naive subjects received a dolutegravir INSTI-containing regimen for 20 weeks (either dolutegravir/abacavir/lamivudine or dolutegravir plus 2 other NRTIs if subjects were HLA-B*5701 positive). Subjects who were virologically suppressed (HIV-1 RNA less than 50 copies/mL, n = 566) were then randomized (1:1) to receive either a cabotegravir plus rilpivirine regimen or remain on the current antiretroviral regimen. Subjects randomized to receive cabotegravir plus rilpivirine initiated treatment with daily oral lead-in dosing with one 30-mg Vocabria (cabotegravir) tablet plus one 25-mg Edurant (rilpivirine) tablet for at least 4 weeks followed by monthly injections with Cabenuva for an additional 44 weeks.
2. Trial 201585 (ATLAS, [NCT02951052]), (n = 616): HIV-1–infected, ART-experienced, virologically-suppressed (for at least 6 months; median prior treatment duration was 4.3 years) subjects (HIV-1 RNA less than 50 copies/mL) were randomized and received either a cabotegravir plus rilpivirine regimen or remained on their current antiretroviral regimen. Subjects randomized to receive cabotegravir plus rilpivirine initiated treatment with daily oral lead-in dosing with one 30-mg Vocabria (cabotegravir) tablet plus one 25-mg Edurant (rilpivirine) tablet for at least 4 weeks followed by monthly injections with Cabenuva for an additional 44 weeks.
3. Trial 207966 (ATLAS-2M, [NCT03299049]), (n = 1,045): HIV-1–infected, ART-experienced, virologically suppressed subjects, including 504 subjects from the ATLAS trial (randomized to CAB plus RPV [n = 253] or CAR [n = 251]; prior exposure to cabotegravir plus rilpivirine [n = 391]), were randomized and received a cabotegravir plus rilpivirine regimen administered as injection doses of cabotegravir 400 mg plus rilpivirine 600 mg either monthly or cabotegravir 600 mg plus rilpivirine 900 mg every 2 months. Subjects without prior exposure to cabotegravir plus rilpivirine initiated treatment with daily oral lead-in dosing with one 30-mg VOCABRIA (cabotegravir) tablet plus one 25-mg Edurant (rilpivirine) tablet for at least 4 weeks followed by monthly or every-2-month injections with Cabenuva for an additional 44 weeks. The primary endpoint of ATLAS-2M was the proportion of subjects with a plasma HIV-1 RNA ≥ 50 copies/mL at Week 48. The primary endpoint was met with 2% of subjects in the every 2-month dosing arm having an HIV-RNA ≥ 50 copies/mL compared to 1% in the monthly dosing arm.

The primary analysis was conducted after all subjects completed their Week 48 visit or discontinued the trial prematurely. The primary endpoint of FLAIR and ATLAS was the proportion of subjects with plasma HIV-1 RNA greater than or equal to 50 copies/mL at Week 48. In both FLAIR and ATLAS 2% of subjects met the primary endpoint as compared to 2% and 1% in the comparator arms respectively. Subjects in both the FLAIR and ATLAS trials were virologically suppressed prior to Day 1 or at study entry, respectively, and no clinically relevant change from baseline in CD4+ cell counts was observed.[1]

In February 2021 and September 2022, the United States Department of Health and Human Services updated their guidelines for the use of antiretroviral agents in adults and adolescents with HIV. The February 2021 update included specific recommendations for use of Cabenuva. The guidelines panel made the following recommendation: “Cabenuva can be used as an optimization strategy for people with HIV currently on oral ART with documented viral suppression for at least 3 months (although optimal

duration is not defined)".[4] In the ATLAS trial, participants had viral suppression for at least 6 months on standard oral ART prior to randomization. A key consideration noted by the guidelines panel includes "experienced participants enrolled in completed clinical trials for Cabenuva were selected based on their history of good adherence and engagement in care, as documented by sustained viral suppression at baseline. Therefore, these therapies are currently recommended for participants who are similarly engaged in care." The Panel does not recommend Cabenuva as initial therapy for people with HIV at this time. The September 2022 update included an a note in the Adherence to the Continuum of Care section that the Panel recommends against the use of the long-acting ART regimen of intramuscular cabotegravir and rilpivirine in people who have detectable viral load due to suboptimal adherence to ART and who have ongoing challenges with retention in HIV care, except in a clinical trial (AIII).

HCPCS Code

HCPCS Code	Description
J0741	Injection, cabotegravir and rilpivirine, 2mg/3mg

Diagnosis Codes

Diagnosis Code	Description
B20	Human immunodeficiency virus [HIV] disease
Z21	Asymptomatic human immunodeficiency virus [HIV] infection status

Dosage form & Route of administration

Concentration	Route
400mg/2ml cabotegravir and 600mg/2ml rilpivirine ER inj suspension	IM injection
600mg/3ml cabotegravir and 900mg/3ml rilpivirine ER inj supsension	IM injection

Acronyms

ART = Antiretroviral Treatment

DNA = Deoxyribonucleic acid

HIV-1 = Human Immunodeficiency Virus 1

INSTI = Integrase strand transfer inhibitor

NNRTI = Non-nucleoside reverse transcriptase inhibitor

RT = Reverse transcriptase

References

1. Cabenuva [package insert]. Research Triangle Park, NC: ViiV Healthcare. February 2023.

2. Swindells S, et al. Long-Acting Cabotegravir and Rilpivirine for Maintenance of HIV-1 Suppression (ATLAS). N Engl J Med. 2020 March 382:1112-1123.

3. Orkin C, et al. Long-Acting Cabotegravir and Rilpivirine after Oral Induction for HIV-1 Infection (FLAIR). N Engl J Med. 2020 March 382:1124-1135.

4. U.S. Department of Health and Human Services. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV. Updated September 21, 2022. Available at: https://clinicalinfo.hiv.gov/sites/default/files/guidelines/documents/adult-adolescent-arv/guidelines-adult-adolescentarv.pdf. Accessed March 22, 2023.